Executive Summary

STEM CELL IMMUNE GENE IMMUNOTHERAPY FOR CURING VIRUS-ASSOCIATED CANCERS

MISSION

The mission of CDR3 Therapeutics is to develop a curative stem cell gene immunotherapy, delivering chimeric antigen receptors (CARs) or T cell receptors (TCRs) to treat virus-associated cancers.

THE SCIENCE AND MEDICINE OF CDR3

VIRUS-ASSOCIATED CANCERS:
Chronic viral infections have drastic consequences on human health and welfare. Some have suppressive but non-curative treatments, such as herpesviruses (HSV-1/2, EBV, CMV) or Hepatitis B Virus infections, while others have no treatments, such as human papillomavirus (HPV). Beyond the clinical and economic burdens of chronic viral infections, many often lead directly or indirectly to cancer.

THE PROMISE:
Researchers have known for decades that T cells are critical for killing cells in the body with foreign or mutated proteins, *i.e.*, cells that are virus-infected or cancerous or chronic viral infections, for cure or containment of disease. T cells use naturally generated T cell receptors (TCRs) to target and kill such abnormal cells. In the past few years, artificial TCRs called chimeric antigen receptors (CARs) have been inserted into patient T cells using gene therapy (T cell immunotherapy), thereby reprogramming them to target cancers. Four CAR gene therapies have been FDA cleared for treatment of blood cancers, and many more are in clinical testing.

THE CHALLENGE:
Clinical success has been achieved for a few diseases that can be rapidly cured with T cell immunotherapy, but most virus-associated cancers and chronic viral infections are resistant to clearance. Such conditions will require sustained and long-lived T cell targeting to control and/or clear disease long term, perhaps over years or decades. Current T cell immunotherapy technology involves extraction of peripheral blood T cells, performing CAR or TCR gene therapy, expanding them to large numbers in the laboratory, and giving them back to patients. This is amenable to short term therapy, but this process drives the cells to become abnormal, with reduced function and poor long-term survival after reinfusion, a significant limitation of the only FDA-cleared CAR therapeutics, Yescarta from Kite, Kymriah from Novartis, and Breyanzi and Abecma from Bristol Myers Squibb.

OUR PROPRIETARY SOLUTION:
We have developed patented and proprietary technology to introduce CARs/TCRs targeting virus-associated cancers into hematopoietic stem cells (HSCs), which are precursor cells that generate all the cells of the immune system. Administered HSCs engraft in the bone marrow and continuously develop normally into functional T cells in the body. Isolating HSCs from patients, applying CAR/TCR gene therapy, and reinfusing them creates a permanent, self-renewing source of healthy, normally developed T cells with the CAR/TCR, avoiding the high cost and significant limitations of expanding T cells outside the body for adoptive T cell gene therapy.

While other CAR-T therapeutic companies are modifying cell death and proliferation pathways or antigen receptor peptide chains, or editing major histocompatibility complex (MHC) genes, their technologies are still limited by low level persistence and reduced function from expansion of retargeted cells outside the patient's body. Thus, our HSC-based technology provides a long-term source for fully functional T cells that have been retargeted against the virus-associated cancer or chronic viral infection, which can be maintained to control or prevent disease for the lifetime of the patient. Our strategy using virus-specific CARs and TCRs delivered via HSCs may also mitigate cytokine release syndrome (CRS), a severe inflammatory and sometimes fatal complication seen with the current FDA-cleared T cell immunotherapies. For experimental proof-of-concept, we have shown in humanized mice (mice transplanted with human immune systems) and monkeys that HSC CAR gene therapy can generate new antiviral T cells in the body that safely persist and have potent effects against HIV.

KEY BENEFITS OF CDR3 TECHNOLOGY

- HSC-based CAR/TCR gene therapy creates a permanent, self-renewing source of T cells directed against diseased cells over the lifetime of the patient compared to the short-term persistence of current CAR therapies
- These T cells are naturally produced in the body and are normal in their ability to function and persist, in contrast to current T cell immunotherapies that grow the cells outside the body
- Eliminates the high cost and biological problems associated with growing cells outside the body
- Potentially removes T cells that target normal cells during T cell development in the body, reducing the risk of CRS associated with conventional CAR therapy
- Addresses the barriers for successful treatment of virus-associated cancers and chronic viral infections that require persistent highly functional T cells, such as Human Papillomavirus (causing cervical cancer, anal cancer, head and neck cancer, tongue/mouth cancer), Cytomegalovirus (CMV), Epstein-Barr Virus (causing post-transplant lymphoproliferative disease, nasopharyngeal carcinoma, and gastric carcinoma), and Hepatitis B Virus.

BUSINESS PLAN

The patented and proprietary technologies developed by CDR3 provide the basis to pursue gene immunotherapies harnessing stem cells to achieve success where current T cell immunotherapies have failed. CDR3 will initially focus its efforts on treatment of HPV-associated cancers using a TCR that is in development and CMV infection during solid organ transplant using a CAR that was developed in the lab of one of our founders. These will be our prototypic first products for investigational new drug (IND) development, establishing a platform that is readily translatable to the treatment of other virus-associated cancers and chronic viral infections. CDR3 has already demonstrated proof-of-concept in extensive HIV preclinical animal testing, producing immunity that can control the virus to obviate the need for life-long treatment with expensive medications that have significant side effects. Our immediate goal is to raise the $3-5 million of initial funds to obtain FDA approval of an IND for Phase I clinical trials of TCR stem cell immunotherapies for HPV-associated cancers.

THE COMPANY

T cell CAR gene immunotherapy has had a huge impact on an extremely limited class of cancers (B cell liquid tumors) but has hit a significant roadblock in treating conditions requiring persisting immunity such as solid tumors. Nonetheless, this has been a high area of growth and investment in the biopharmaceutical area. CDR3 Therapeutics' uniqueness lies in its ability to address this critical issue through patented technology to harness stem cells, and we are uniquely positioned to capitalize on this trend for patients and investors alike. Based on decades of research, we have developed CARs and techniques to apply to HIV as a proof-of-concept with strong pre-clinical data supporting the success of our approach.

CDR3 Therapeutics is a Delaware Corporation with three of its scientist-founders located at the University of California, Los Angeles. They have over 20 years' experience working together on HIV research and garnered more than $96 million in peer-reviewed grants from the National Institutes of Health (NIH) and the California Institute for Regenerative Medicine (CIRM). They hold two core issued patents and one core application filed by UCLA Technology Development Group (TDG), and CDR3 holds an exclusive license from The Regents of The University of California for these proprietary technologies.

The CDR3 Company Founders and Management Team:

Scott G. Kitchen, PhD - UCLA Associate Professor of Medicine. Dr. Kitchen is a biomedical, translational scientist who developed much of the platform on which the CDR3 CAR technology is based. He has vast expertise in immunotherapy development and in the development of stem cell-based technologies.

Otto O. Yang, MD - UCLA Professor of Medicine. Dr. Yang is a physician-scientist whose expertise spans both clinical infectious diseases and translational laboratory research. His interests include the HIV pathogenesis and the role of cellular immunity in infections, transplantation, and malignancies, with emphasis on developing immunotherapeutic strategies.

Jerome A. Zack, PhD - UCLA Distinguished Professor of Medicine and Chair of Microbiology, Immunology, and Molecular Genetics. Dr. Zack is a biomedical scientist who has extensive experience in the development of new ways to understand and attack viral infection, particularly that of HIV, and in stem cell-based approaches.

Matthew C. Lorence, PhD, MBA - Chief Executive Officer. Dr. Lorence is a biomedical scientist and business professional with extensive commercial experience in the genomics and molecular diagnostic industries and has extensive FDA experience.

For more information about CDR3 Therapeutics and its mission to provide curative stem cell-based gene immunotherapies, contact Matthew Lorence at mclorence@cdr3tx.com.